

Application Serial No.: 10/030,605

IN THE CLAIMS:

1. (Currently amended) A protein ~~Protein~~ with beta-sheet structure, wherein amino acids ~~exposed on a surface of the protein located within~~ at least two β -strands ~~exposed on a surface of at least one beta sheet exposed on a surface of the protein~~ are mutagenized, wherein the mutagenizing is selected from the group consisting of an insertion, a deletion, a substitution, and combinations thereof, such that the protein has a new property, ~~wherein the new property is selected from the group consisting of an antigen binding specificity, a catalytic activity, and a fluorescence property, and combinations thereof, with the proviso that:~~

- (i) the protein without substitution, deletion, or insertion has no binding activity, catalytic activity, or fluorescence property at the surface of the beta-sheet structure wherein the amino acids are mutagenized, and after substitution, deletion, or insertion at the surface of the beta-sheet structure, the protein has the new property selected from the group consisting of an antigen binding specificity, a catalytic activity, a fluorescence property, and combinations thereof; or
- (ii) the protein has a binding activity, catalytic activity, or fluorescence property before the substitution, deletion, or insertion, and that after the substitution, deletion, or insertion at the surface of the beta-sheet structure, the protein has an additional new binding activity, an additional new catalytic activity, an additional new fluorescence property, or combinations thereof.

2. (Currently amended) ~~Protein according to~~ The protein of Claim 1, wherein the protein to be mutagenized is selected from the group consisting of a crystalline crystallin, a spheruline, a heat shock protein, a cold shock protein, a β -helix protein, a lipocalin, a serpin, a fibronectin, a transcription factor, a green

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fluorescent protein (GFP), a nerve growth factor (NGF), a tendamistat, and a lysozyme.

3. (Currently amended) ~~Protein according to~~ The protein of Claim 1, wherein amino acids ~~exposed on the surface of~~ located within three beta strands exposed on the surface of the protein are mutagenized.

4. (Currently amended) ~~Protein according to~~ The protein of Claim 1, wherein amino acids ~~exposed on the surface of~~ located within at least four beta strands exposed on the surface of the protein are mutagenized.

5. (Currently amended) ~~Protein according to~~ The protein of claim 1, wherein amino acids ~~exposed on the surface of~~ located within at least two beta strands of at least two beta sheets of the protein are mutagenized.

6. (Currently amended) ~~Protein according to~~ The protein of claim 1, wherein amino acids ~~exposed on the surface of~~ located within three beta strands of two antiparallel beta sheets of the protein are mutagenized.

7. (Currently amended) ~~Protein according to~~ The protein of claim 1, wherein the protein is a vertebrate ~~crystalline~~ crystallin.

8. (Currently amended) ~~Protein according to~~ The protein of claim 1, wherein the protein is selected from the group consisting of an alpha-~~crystalline~~ crystallin, a beta-~~crystalline~~ crystallin, and a gamma-~~crystalline~~ crystallin.

9. (Currently amended) ~~Protein according to~~ The protein of claim 1, wherein the protein is a gamma-II-~~crystalline~~ crystallin.

10. (Currently amended) ~~Protein according to~~ The protein of claim 1, wherein an amino acid ~~exposed on the surface of~~ located within the protein is mutagenized in a region of the beta sheet that is accessible to a solvent.

11. (Currently amended) ~~Protein according to~~ The protein of claim 1, wherein an amino acid ~~exposed on the surface is~~ mutagenized in a region of the protein selected from the group consisting of a β -sheet structure of a domain of the protein and a β -sheet structure of a subunit of the protein.

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12. (Currently amended) ~~Protein according to~~ The protein of claim 9, wherein at least one of the amino acids Lys ~~[[2]]~~ 3, Thr ~~[[4]]~~ 5, Tyr ~~[[6]]~~ 7, Cys ~~[[15]]~~ 16, Glu ~~[[17]]~~ 18, Ser ~~[[19]]~~ 20, Arg ~~[[36]]~~ 37, and Asp ~~[[38]]~~ 39 of a bovine gamma-II-crystalline ~~crystallin of SEQ ID NO: 22~~ is mutagenized.

13. (Currently amended) ~~Protein according to~~ The protein of claim 1, ~~wherein an amino acid exposed on the surface of the protein is mutagenized in the beta sheet such that the protein has a new property,~~ wherein the new property is selected from the group consisting of an antigen binding specificity and a catalytic activity.

14. (Currently amended) ~~Protein according to~~ The protein of Claim [[13]] 1, wherein the new ~~property is an~~ antigen binding specificity is for a compound selected from the group consisting of estradiol and BSA- β -estradiol-17-hemisuccinate.

15. (Currently amended) ~~Protein according to~~ The protein of claim 1, wherein the protein has a new antigen binding specificity for a compound selected from the group consisting of estradiol and BSA- β -estradiol-17-hemisuccinate, and wherein the protein has an amino acid sequence comprising one of SEQ ID NO: 19 and SEQ ID NO: 21.

16. (Currently amended) A composition comprising a the protein according to ~~to~~ of claim 1 and at least one other protein or non-protein substance.

17. (Withdrawn) DNA coding for a protein according to claim 1.

18. (Withdrawn) RNA derived from the DNA according to claim 17.

19. (Cancelled)

20. (Withdrawn) Method for preparing the protein of claim 1, the method comprising:

- (a) mutagenizing a DNA coding for a protein with beta-sheet structure in those regions which code for at least two beta strands, exposed on the surface, of a beta sheet exposed on the surface;
- (b) expressing the DNA obtained in step (a) in an expression system to produce a protein encoded by the expressed DNA;

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- (c) selecting a protein encoded by the expressed DNA having a desired property; and
- (d) isolating the protein encoded by the expressed DNA having the desired property.

21. (Withdrawn) Method according to Claim 20, wherein the mutagenizing comprises a site-specific substitution in the beta sheet.

22. (Withdrawn) Method according to claim 20, wherein the expressing is in a system selected from the group consisting of a prokaryotic cell, a eukaryotic cell, and a cell-free system.

23. (Withdrawn) Method according to claim 20, further comprising identifying a protein having a desired property by contacting the protein with a binding partner, wherein the binding of the protein to the binding partner identifies the protein as having the desired property.

24. (Withdrawn) Method according to claim 20, wherein the desired property of the protein is a catalytic activity and wherein identifying the protein having a desired catalytic activity comprises contacting the protein encoded by the expressed DNA with a substrate, wherein the binding of the protein encoded by the expressed DNA to the substrate identifies the protein encoded by the expressed DNA as having the desired catalytic activity.

25. (Withdrawn) A method of preparing a composition for use in an application selected from the group consisting of diagnostics, therapy, cosmetics, bioseparation, biosensors, and reducing harmful substances, the method comprising:

- (a) providing a protein according to claim 1; and
- (b) preparing a composition for use in an application selected from the group consisting of diagnostics, therapy, cosmetics, bioseparation, biosensors, and reducing harmful substances by incorporating therein the protein according to claim 1.

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26. (Currently amended) ~~Protein according to~~ The protein of claim 7, wherein the vertebrate is selected from the group consisting of a bovine, a rodent, a bird, and a fish.

27. (Currently amended) ~~Protein according to~~ The protein of claim 1, wherein an amino acid ~~exposed on the surface~~ of the protein is mutagenized in a region of the beta sheet that is accessible to a binding partner.

28. (Currently amended) ~~Protein according to~~ The protein of claim 1, wherein an amino acid ~~exposed on the surface~~ is mutagenized in a β -sheet structure of a subunit of the protein.

29. (Withdrawn) The method of claim 20, further comprising purifying the protein encoded by the expressed DNA.

30. (Withdrawn) The method of claim 20, wherein the expressing is on the surface of an entity selected from the group consisting of a plant cell, an animal cell, a yeast cell, a virus, and a bacterium.

31. (Withdrawn) The method according to Claim 20, wherein the mutagenizing comprises a site-specific deletion in the beta sheet.

32. (Withdrawn) The method according to Claim 20, wherein the mutagenizing comprises a site-specific insertion in the beta sheet.

33. (Withdrawn) The method according to Claim 20, wherein the mutagenizing comprises a random substitution in the beta sheet.

34. (Withdrawn) The method according to Claim 20, wherein the mutagenizing comprises a random deletion in the beta sheet.

35. (Withdrawn) The method according to Claim 20, wherein the mutagenizing comprises a random insertion in the beta sheet.

36. (Withdrawn) A vector comprising the DNA of claim 17.

37. (Withdrawn) The vector of claim 36, wherein the vector is a prokaryotic vector.

38. (Withdrawn) The vector of claim 36, wherein the vector is a eukaryotic vector.

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39. (Withdrawn) The vector of claim 36, wherein the DNA has a nucleotide sequence that encodes a protein having an amino acid sequence that is one of SEQ ID NO: 19 and SEQ ID NO: 21.

40. (Withdrawn) A cell comprising the DNA of claim 17.

41. (Withdrawn) The cell of claim 40, wherein the DNA has a nucleotide sequence that encodes a protein having an amino acid sequence that is one of SEQ ID NO: 19 and SEQ ID NO: 21.

42. (Currently amended) A mutagenized gamma ~~crystalline~~ crystallin polypeptide, wherein the mutagenizing is selected from the group consisting of an insertion, a deletion, a substitution, and combinations thereof, such that the gamma ~~crystalline~~ crystallin polypeptide has a new binding property.

43. (Withdrawn) A method for preparing a gamma crystalline protein with a new binding property, the method comprising mutagenizing a gamma crystalline polypeptide, wherein the mutagenizing is selected from the group consisting of an insertion, a deletion, a substitution and combinations thereof, to provide a mutagenized gamma crystalline protein with a new binding property.

44. (Withdrawn) A method of preparing a protein with a new binding property, the method comprising:

- (a) mutagenizing a gamma crystalline protein to provide a gamma crystalline protein with a new binding property; and
- (b) combining the mutagenized gamma crystalline protein with another protein to provide a protein with a new binding property.

45. (Withdrawn) The method according to claim 44, wherein the mutagenizing is selected from the group consisting of an insertion, a deletion, a substitution and combinations thereof.